



the criticism that there may have been a reasonable expectation of success after publication and before invention. Under the scenario posed by the Examiner's supplemental answer, the only pertinent evidence would be a publication at the date of invention. It is submitted that this would be an unreasonable standard.

Secondly, the Supplemental Examiner's Answer takes the position that the test of Yamamoto was to confirm a reasonable expectation. A reading of Yamamoto indicates confirmation was not the purpose of the test, but rather to establish whether selective inhibitors of COX-2 would prevent cirrhosis. Consider the following language in the first paragraph under "Discussion" in Yamamoto et al.

Previous studies showed that the nonselective COX inhibitors piroxicam and acetylsalicylic acid prevented cirrhosis and development of preneoplastic nodules in CDAA-treated rats. 18,33 One of the aims of our study was to examine whether selective inhibition of COX-2 alone would be sufficient to realize this goal because such inhibition appears to yield much less toxicity than other nonsteroidal anti-inflammatory drugs.

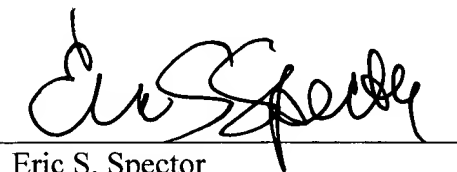
In other words, testing was necessary to exclude the need of significant COX-1 inhibition to obtain cirrhosis preventing effect.

Reversal of the rejection is requested.

Respectfully submitted,

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